UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/781,592	02/12/2001	Beverly M. Emerson	1211.003US1	1304

7590 01/13/2003

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. Box 2938
Minneapolis, MN 55402

EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1635	12

DATE MAILED: 01/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/781,592	EMERSON, BEVERLY M.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-88* is/are pending in the application.

4a) Of the above claim(s) *52,62,78 and 86* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-43,48-51,53-61,63-69,74-77,79-85,87-88* is/are rejected.

7)☒ Claim(s) *44-47 and 70-73* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 February 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Non-Final Rejection

Claims 38-88 are pending examination.

Applicant's election with traverse of Group I in Paper No. 11 is acknowledged. The traversal is not based on any ground(s). This is not found persuasive because the applicant did not point out the supposed errors with the restriction.

The requirement is still deemed proper and is therefore made FINAL.

Claims 52, 62, 78, 86 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 11.

The international search report has been considered.

Claim Objections

Claims 57 and 83 are objected to because of the following informalities: a bracket after the word "LCR". Suggest replacing the bracket with a closed parenthesis ")". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38-43, 48-51, 53-61, 63-69, 74-77, 79-85, 87-88 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 38-43, 48-51, 53-61, 63-69, 74-77, 79-85, 87-88 as best understood, are readable on a genus of subunits of chromatin remodeling complex associated with a domain of a nucleic acid regulatory protein, wherein the genus of one or more subunits of chromatin remodeling complex associated with a domain of a nucleic acid regulatory protein is not claimed in a specific biochemical or molecular structure that could be envisioned by one skilled in the art at the time the invention was made are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 38, 60, 61, 63, and 84-85 as best understood, are readable on a genus of test compound that is a small molecule or a peptide, wherein the genus of test compounds is not claimed in a specific biochemical or molecular structure that could be envisioned by one skilled in the art at the time the invention was made are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification contemplates using a genus of one or more subunits of chromatin remodeling complex associated with a domain of a nucleic acid regulatory protein. The as-filed specification provides sufficient description of a chromatin remodeling complexes selected from SWI/SNF, RSC, NURF, CHRAC, ACF, NURD, and RSF. The specification and state of the art provide sufficient description of SWI/SNF subunits associated with a domain of nucleic acid regulatory proteins (e.g. transcription factor). However, the specification does not provide sufficient description of a representative number of subunits of other chromatin remodeling complexes that associated with a domain of a nucleic acid regulatory protein. The specification states that, "there are seven chromatin-remodeling complexes and several properties indicate that these complexes are functionally and mechanistically distinct" (page 3). In addition, the art of record states, "the process by which SWI/SNF and other chromatin remodeling complexes activate specific subsets of genes is poorly understood" (IDS, Kadam et al., Genes & Development, 14:2441-2451, 2000).

It is apparent that on the basis of applicant's disclosure, an adequate written description of the invention defined by the claims requires more than a mere statement that it is part of the invention and reference to potential methods and/or molecular structures of molecules that are essential for the genus of one or more subunits of chromatin remodeling complex associated with a domain of a nucleic acid regulatory protein as claimed; what is required is the knowledge in the prior art and/or a description as to the availability of a representative number of species of biochemical or molecular structures of one or more subunits of a chromatin remodeling complex that must exhibit the disclosed biological functions as contemplated by the claims.

Furthermore, the specification contemplates using a genus of test compound selected from small molecules and peptides, however, it is apparent that on the basis of applicant's disclosure, an adequate written description of the invention defined by the claims requires more than a mere statement that it is part of the invention and reference to molecular structures of molecules that are essential for the genus of test compounds as claimed; what is required is the knowledge in the prior art and/or a description as to the availability of a representative number of species of biochemical or molecular structures of test compounds that must exhibit the disclosed biological functions as contemplated by the claims.

It is not sufficient to support the present claimed invention directed to a genus of one or more subunits of chromatin remodeling complex associated with a domain of a nucleic acid regulatory protein and/or a genus of test compounds selected from peptides and small molecules. The claimed invention as a whole is not adequately described if the claims require essential or critical elements, which are not adequately described in the specification and which is not conventional in the art as of applicant's effective filing date. Claiming an unspecified genus of peptides or small molecules and/or genus of one or more subunits of a chromatin remodeling complexes that must possess the biological properties as contemplated by applicant's disclosure without defining what means will do so is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the

inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structure of a genus of test compounds selected from peptides or small molecules and/or genus of the claimed one or more subunits of a chromatin remodeling complexes that must exhibit the contemplated biological functions, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in the as-filed specification. Thus, in view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

Claims 38-43, 48-51, 53-61, 63-69, 74-77, 79-85, 87-88 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method to identify a test compound that modulates the chromatin remodeling complex (SWI/SNF), does not reasonably provide enablement for using a genus of one or more subunits of chromatin remodeling complex associated with a domain of a nucleic acid regulatory protein or using a genus of test compounds selected from small molecules and peptides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Specifically, since the claimed invention is not supported by a sufficient written description (for possession of a genus of one or more subunits of a chromatin remodeling complexes associated with a domain of a nucleic acid regulatory protein and/or a genus of test compounds selected from a small molecule or a peptide), particularly in view of the reasons set

forth above, one skilled in the art would not have known how to use and make the claimed invention so that it would operate as intended, e.g. used to identify a test compound that modulates chromatin remodeling of a specific DNA sequence within chromatin.

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The invention is directed to methods of identifying test compounds for modulating chromatin remodeling of a specific DNA sequence within chromatin.

The art of record states, "the process by which SWI/SNF and other chromatin remodeling complexes activate specific subsets of genes is poorly understood" (IDS, Kadam et al).

In addition, the art of record displays that, "little is known about the manner in which remodeling complexes disrupt nucleosomes" and "mechanism to explain gene regulation have become increasingly sophisticated over the past few years" and "challenges will be how to decipher how remodeling and modification machinery modulate the nucleosomal structure of heterochromatin, centromeres, and telomeres as well as regulate distinct nuclear processes" (IDS, Armstrong et al. Curr. Opin. Genet. Dev. 8:165-172, 1998).

The as-filed specification teaches:

> Mammalian SWI/SNF complexes exist in broad classes depending on whether they contain the subunit BRG1 or BRM as their DNA-dependent ATPase. Zinc finger DNA-binding domain specificity is only achieved with BRG1-containting SWI/SNF complexes. BRM complexes presumably interact with another class of transcription factors. This is very advantageous because it further demonstrates the degree of specificity that chromatin-remodeling complexes employ to regulate distinct subsets of genes (page 10).

Thus, making and using a genus of chromatin remodeling complexes associated within a domain of a nucleic acid regulatory protein is considered highly unpredictable.

The specification teaches *in vitro* experiments that demonstrate how mammalian chromatin remodeling complexes (SWI/SNF) regulate transcription (Example 1, pages 18-19). Furthermore, the specification teaches that SWI/SNF selectively functions with several zinc finger DNA-binding proteins to remodel chromatin and activate transcription in vitro (pages 19-21). Example 2, a pharmaceutical screening protocol is contemplated the claimed methods (pages 26-29). Example 3, the specification teaches that activation of repressed genes by facilitated protein binding through targeted chromatin remodeling by zinc finger protein motifs and SWI/SNF (pages 29-30). Example 4, the specification uses an assay to display that either β-globin gene with SWI/SNF + EKLF or the gamma-globin gene are differently activated with a novel protein complex and this assay can be used as a high-throughput drug screening assay (page 30). Example 5, the specification teaches an in vitro assay has been developed that reproduced p-53 dependent activation of the p21 cell cycle inhibitor gene and this assay can be used for high-throughput screening of drugs that enhance or interfere with protein interaction (pages 31-32).

The specification provides sufficient guidance for one skilled in the art to make and use one or subunit from SWI/SNF associated with domains from different regulatory proteins, but does not provide sufficient guidance or factual evidence for the full scope of the claimed embodiment. The specification contemplates using subunits associated with a domain of a nucleic acid regulatory protein from a genus of chromatin remodeling complexes and list several chromatin complexes. However, the specification only discloses domains of nucleic acid regulatory proteins that associate with subunits from SWI/SNF (pages 8-9). The state of the art at the time the application was filed displays that there are numerous distinct nucleic acid

regulatory proteins and SWI/SNF has been found to associate with diverse regulators of gene activation and cell proliferation (Kadam, pages 2441-2451). Furthermore, several chromatin-remodeling complexes are considered newly discovered (ACF, CHRAC) and the association between subunits of these complexes and nucleic acid regulatory proteins is not certain (Armstrong, pages 166-167). Armstrong also states that, "new chromatin remodeling complex, FACT found in humans appears to function quite distinctly from other chromatin remodeling complexes as it does not facilitate transcription initiation or require ATP hydrolysis" (page 167). In view of the In Re Wands Factors, the as-filed specification does not provide sufficient guidance for what subunits of other chromatin remodeling complexes are associated with a domain of any nucleic acid regulatory protein.

In addition, in view of the breadth of the genus of chromatin remodeling complexes from different organism (yeast, Drosophila, human, etc.) that have not been disclosed by the specification and are absent from the art of record (See Armstrong pages 166-167), the specification does not provide a representative number from each genus of chromatin remodeling complex for one skilled in the art to practice the genus of chromatin remodeling complexes recited in the claims.

As a result, it is not apparent how one skilled in the art determines, without undue experimentation, how to reasonably correlate from the chromatin remodeling complex, SWI/SNF to the genus of chromatin remodeling complex (e.g. Armstrong pages 166, teaches that, "in a transcriptional assay NURF cannot be replaced by either yeast SWI/SNF or CHRAC"), how is it apparent as to how one skilled in the art, without any undue experimentation, practices the full breadth of any method as contemplated by the claims, particularly given the unpredictability of

making and using a genus of chromatin remodeling complexes associated within a domain of a nucleic acid regulatory protein and/or the doubts expressed in the art of record.

In conclusion, the as-filed specification and claims coupled with the state of the art at the time the invention was made lack sufficient guidance and/or evidence to reasonably enable the full breadth of the claimed invention. Given that there is no representative number of test compounds selected from a peptide or small molecule that could be used in any method to modulate any interaction of a subunit of a chromatin remodeling complex and a domain within a nucleic acid regulatory protein. In addition, since the disclosure does not provide sufficient guidance for what, one skilled in the art would have to engage in a large quantity of experimentation in order to practice the claimed invention based on the applicant's disclosure and the unpredictability of using a genus of chromatin remodeling complexes associated with a domain of a nucleic acid regulatory protein.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 60 and 84 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "small molecule" in claims 60 and 84 is a relative term, which renders the either claim indefinite. The term "small molecule" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The disclosure does not define

the metes and bounds of the term. One skilled in the art understands that there are molecules that are considered a small molecule (e.g. DNA, RNA, organic compound, peptide, inorganic compounds, etc.) and the disclosure does not claim or particularly point out what is a small molecule.

Claims 44-47 and 70-73 are objected to as being dependent upon a rejected base claim (claims 38 and 63), but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader, SPE - Art Unit 1635, can be reached at (703) 308-0447.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Brian Whiteman
Patent Examiner, Group 1635
1/10/03

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER